WE CLAIM:

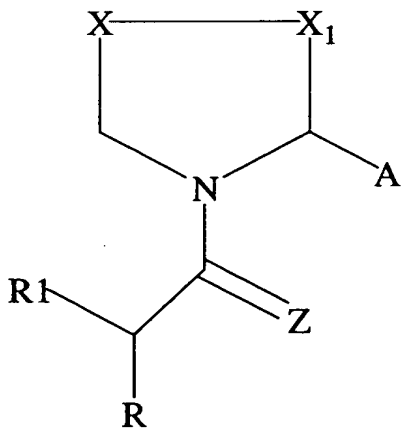
1. An inhibitor of dipeptidyl peptidase IV, wherein the inhibitor comprises a proline mimetic and possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

2. The inhibitor according to claim 1, wherein the IC_{50} is no more than 100 nm.

3. The inhibitor according to claim 1, wherein the inhibitor can be used to treat a central nervous system disorder selected from the group consisting of strokes, tumors, ischemia, Parkinson's disease, amyotrophic lateral sclerosis and migraines.

4. A reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(I)



, wherein:

X is CR2R3, O, S, or NR4; with the proviso that if X is S, or if X and X1 are both CH_2, and Z is O, and A is CN, and R1 is H, then R is not NH substituted with C1-C9 straight or branched chain alkyl, or NH substituted with C3-C7 cycloalkyl;

X_1 is CR2R3, O, S, or NR4 with the proviso that X and X1 cannot both be a heteroatom, and with the proviso that if X and X1 are both CH_2, and Z is O, and R1 is NH_2, then R is not 1-methylpropyl if A is COOH, and R is not cyclopentyl if A is CN;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides, with the proviso that if A is CN, and R1 is NH_2, and Z is O, and R is 1-methylpropyl, then X and X1 are not both CH_2; X and X1 are not S; and X is not O;

Z is O or S;

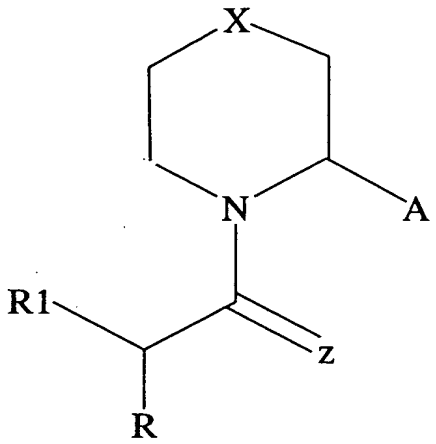
R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

5. The reversible inhibitor according to claim 4, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

6. A reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(II)



, wherein:

X is CR2R3, O, S, or NR4;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

Z is O or S;

R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

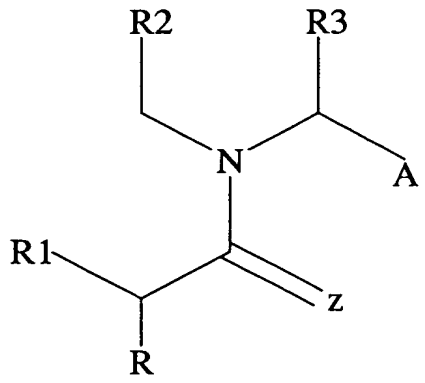
R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol,

trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

7. The reversible inhibitor according to claim 6, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

8. A reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(III)



, wherein:

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

Z is O or S;

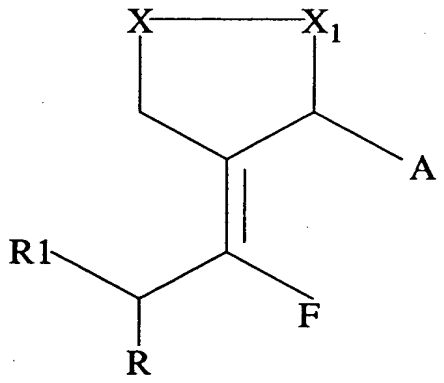
R, R1, R2 and R3 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R, R1, R2 and R3 can be the same or different; and

R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R4, R5, R6 and R7, if present, can be the same or different.

9. The reversible inhibitor according to claim 8, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

10. A reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(IV)



, wherein:

X is CR2R3, O, S, or NR4;

X_1 is CR2R3, O, S, or NR4 with the proviso that X and X1 cannot both be a heteroatom;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

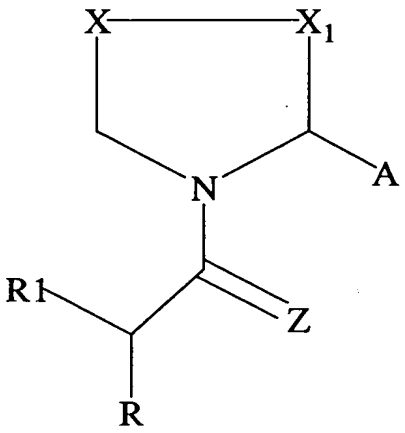
R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

11. The reversible inhibitor according to claim 10, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

12. A method of treating a patient having a disorder of the central nervous system, comprising administering to the patient a therapeutically effective amount of a reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(I)



, wherein:

X is CR2R3, O, S, or NR4;

X_1 is CR2R3, O, S, or NR4 with the proviso that X and X1 cannot both be a heteroatom;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

Z is O or S;

R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-

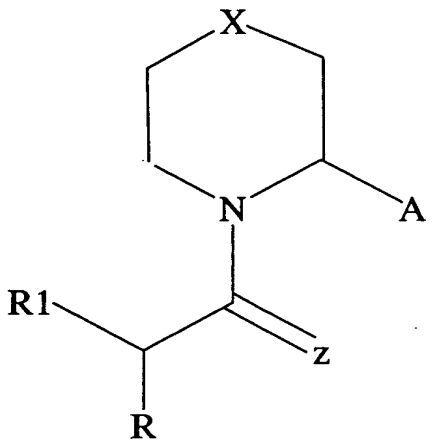
C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

13. The method according to claim 12, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

14. The method according to claim 12, wherein if X is S, or if X and X1 are both CH_2, and Z is O, and A is CN, and R1 is H, then R is not NH substituted with C1-C9 straight or branched chain alkyl, or NH substituted with C3-C7 cycloalkyl; and if X and X1 are both CH_2, and Z is O, and R1 is NH_2, then R is not 1-methylpropyl if A is COOH, and R is not cyclopentyl if A is CN; and if A is CN, and R1 is NH_2, and Z is O, and R is 1-methylpropyl, then X and X1 are not both CH_2; X and X1 are not S; and X is not O;

15. A method of treating a patient having a disorder of the central nervous system, comprising administering to the patient a therapeutically effective amount of a reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(II)



, wherein:

X is CR2R3, O, S, or NR4;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

Z is O or S;

R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

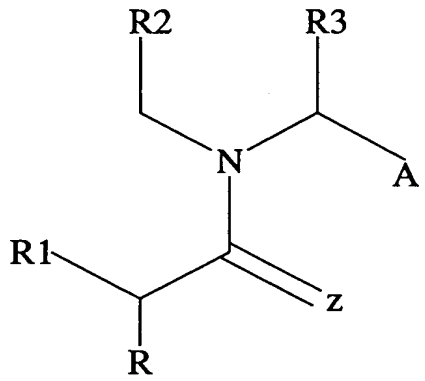
R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy,

C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

16. The method according to claim 15, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

17. A method of treating a patient having a disorder of the central nervous system, comprising administering to the patient a therapeutically effective amount of a reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(III)



, wherein

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

Z is O or S;

R, R1, R2 and R3 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy,

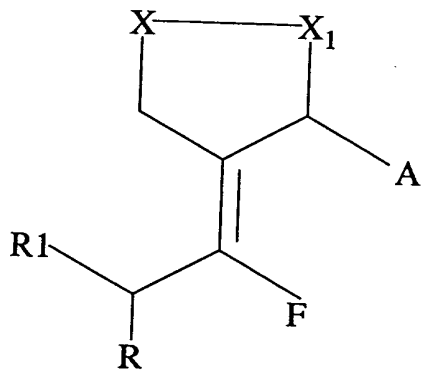
phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R, R1, R2 and R3 can be the same or different; and

R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R4, R5, R6 and R7, if present, can be the same or different.

18. The method according to claim 17, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

19. A method of treating a patient having a disorder of the central nervous system, comprising administering to the patient a therapeutically effective amount of a reversible inhibitor of dipeptidyl peptidase IV, wherein the inhibitor has a core structure of:

(IV)



, wherein:

X is CR2R3, O, S, or NR4;

X_1 is CR2R3, O, S, or NR4 with the proviso that X and X1 cannot both be a heteroatom;

A is H, COOH, or isosteres of carboxylic acids, such as one selected from the group consisting of CN, SO_3H, CONOH, PO_3R5R6, SO_2NHR7, tetrazole, amides, esters, and acid anhydrides;

R and R1 are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R and R1 can be the same or different; and

R2, R3, R4, R5, R6 and R7, if present, are independently selected from the group of functional groups consisting of H, C_1-C_9 branched or straight chain alkyl, C_2-C_9 branched or straight chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl and amino, wherein any of the functional groups can be substituted with one or more of C_1-C_9 straight or branched chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, C_3-C_8 cycloalkyl, cyano, amido, thiol, trifluromethyl, or hydroxy, wherein each of R2, R3, R4, R5, R6 and R7, if present, can be the same or different.

20. The method according to claim 19, wherein the inhibitor possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 500.

21. A method of treating a patient having a disorder of the central nervous system, comprising administering to the patient a therapeutically effective amount of a inhibitor of dipeptidyl peptidase IV.

22. The method according to claim 21, wherein the inhibitor comprises a proline mimetic and possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 700.

23. The method according to claim 21, wherein the inhibitor has a core structure selected from the group consisting of Core Structure I, Core Structure II, Core Structure III and Core Structure IV.

24. The method according to claim 21, wherein the inhibitor is reversible.

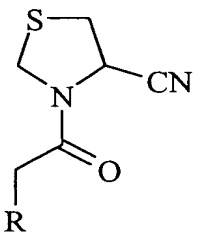
25. The method according to claim 21, wherein the central nervous system disorder is selected from the group consisting of strokes, tumors, ischemia, Parkinson's disease, amyotrophic lateral sclerosis and migraines.

26. A method of treating a patient having a disorder selected from the group consisting of strokes, tumors, ischemia, Parkinson's disease, memory loss, hearing loss, vision loss, migraines, brain injury, spinal cord injury, Alzheimer's disease, amyotrophic lateral, multiple sclerosis, diabetic neuropathy and prostate abnormalities, wherein the method comprises administering to the patient a therapeutically effective amount of a inhibitor of dipeptidyl peptidase IV.

27. A method according to claim 26, wherein the inhibitor comprises a proline mimetic and possesses an IC_{50} of no more than 1 μm and has a molecular weight of no more than 700.

28. The method according to claim 26, wherein the inhibitor has a core structure selected from the group consisting of Core Structure I, Core Structure II, Core Structure III and Core Structure IV.

29. A method of using a reversible inhibitor of DPP-IV, comprising administering to a human patient suffering from a central nervous system disorder a pharamceutically effective amount of the inhibitor, wherein the inhibitor is



wherein R is NH-R^{I};

R^{I} is: C_1 – C_{12} straight or branched chain alkyl;

C_3 – C_7 cycloalkyl;

CH_2- CH_2-NH-R^{II};

CH_2- CH_2-R^{III};

CH_2- CH_2-CHR^{IV}- R^{IV}; or

CH_2- CH_2-CH_2-R^{V};

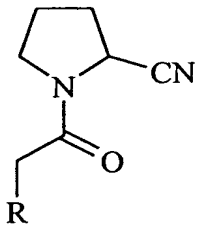
R^{II} is a pyridine ring optionally substituted in one or two positions with halo, trifluoromethyl, cyano or nitro; or a pyrimidine ring optionally substituted in one position with halo, trifluromethyl, cyano or nitro;

R^{III} is a phenyl ring optionally substituted in one to three positions with halo or C_1 – C_3 alkoxy;

Each R^{IV} is independently a phenyl ring optionally substituted in one position with halo or C_1 – C_3 alkoxy; and

R^{V} is a 2-oxopyrrolidine group or a C_2 – C_4 alkoxy group.

30. A method of using a reversible inhibitor of DPP-IV, comprising administering to a human patient suffering from a central nervous system disorder a pharamceutically effective amount of the inhibitor, wherein the inhibitor is



wherein R is NH-R^I;

R^I is: C_1 – C_{12} straight or branched chain alkyl optionally substituted with hydroxy, acetyl, C_1 – C_3 alkoxy, or C_1 – C_3 hydroxyalkyl;

C_3 – C_{12} cycloalkyl optionally substituted with hydroxyl, acetyl, C_1 – C_3 alkoxy, or C_1 – C_3 hydroxyalkyl;

adamantyl; indanyl; piperidyl optionally substituted with benzyl; pyrrolidine optionally substituted with benzyl; bicycloheptyl optionally substituted in one to three positions with methyl; phenyl optionally substituted with in one to three positions with halo, methoxy, trifluoromethyl; pyridyl optionally substituted in one to three positions with halo, trifluoromethyl, nitro; or pyrimidyl optionally substituted with halo, trifluoromethyl, nitro;

C_1 – C_3 straight or branched chain alkyl substituted with R^{IV} , and optionally substituted with hydroxy; or

$(CH_2)_{1-3}$ - $NR^{II}R^{III}$;

R^{II} is hydrogen or methyl;

R^{III} is phenyl optionally substituted with CN, or pyridyl optionally substituted with CN; and

R^{IV} is a group selected from phenyl, naphthyl, cyclohexenyl, pyridyl, pyrimidyl, adamantyl, phenoxy, wherein the group is optionally substituted in one to two positions with ethoxy, methoxy, halo, phenylsulfide, or phenylsulfide substituted with hydroxymethyl.